

Federal State Budgetary Educational Institution of Higher Education  
"Privolzhsky Research Medical University"  
Ministry of Health of the Russian Federation

**BANK OF ASSESSMENT TOOLS FOR DISCIPLINE**

Name of the academic discipline: **BASICS OF PHARMACOGENETICS**

Specialty: **31.05.03 DENTISTRY**

Qualification: **DENTIST**

Department: **GENERAL AND CLINICAL PHARMACOLOGY**

Mode of study: **FULL-TIME**

Nizhniy Novgorod  
2021

### 1. Bank of assessment tools for the current monitoring of academic performance, mid-term assessment of students in the discipline

This Bank of Assessment Tools (BAT) for the discipline "BASICS OF PHARMACOGENETICS" is an integral appendix to the working program of the discipline "Name of discipline/ practice". All the details of the approval submitted in the WPD for this discipline apply to this BAT.

*(Banks of assessment tools allow us to evaluate the achievement of the planned results stated in the educational program.*

*Assessment tools are a bank of control tasks, as well as a description of forms and procedures designed to determine the quality of mastering study material by students.)*

### 2. List of assessment tools

The following assessment tools are used to determine the quality of mastering the academic material by students in the discipline/ practice:

No.	Assessment tool	Brief description of the assessment tool	Presentation of the assessment tool in the BAT
1	Test	A system of standardized tasks that allows you to automate the procedure of measuring the level of knowledge and skills of a student	Bank of test tasks
2	Situational tasks	A method of control that allows you to assess the criticality of thinking and the degree of the material comprehension, the ability to apply theoretical knowledge in practice.	List of tasks
3	Project	The final product obtained as a result of planning and execution of a complex of educational and research tasks. It allows students to evaluate the ability to independently construct their knowledge in the process of solving practical tasks and problems, navigate the information space and the level of formation of analytical, research skills, practical and creative thinking skills. It can be performed individually or by a group of students	Topics of group and/or individual projects

### 3. A list of competencies indicating the stages of their formation in the process of mastering the educational program and the types of evaluation tools

Code and formulation of competence*	Stage of competence formation	Controlled sections of the discipline	Assessment tools
UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)	Entry, Current, Mid-term	Introduction. Subject and scientific and practical tasks of pharmacogenetics.	<i>Tests, situational tasks, projects</i>

UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)	Entry, Current, Mid-term	Genetic factors affecting the pharmacokinetics of drugs	<i>Tests, situational tasks, projects</i>
UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)	Entry, Current, Mid-term	Genetic factors affecting the pharmacodynamics of drugs	<i>Tests, situational tasks, projects</i>
UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)	Entry, Current, Mid-term	Pharmacogenetics of psychotropic drugs	<i>Tests, situational tasks, projects</i>
UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)	Entry, Current, Mid-term	Pharmacogenetic bases of differentiated use of drugs that affect the functions of the digestive system, regulate metabolic processes, inhibit inflammation and affect immune processes	<i>Tests, situational tasks, projects</i>
UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)	Entry, Current, Mid-term	Pharmacogenetic bases of differentiated use of antimicrobial and antiparasitic drugs	<i>Tests, situational tasks, projects</i>

#### 4. The content of the assessment tools of entry, current control

*the bank of assessment tools for conducting current control and mid-term assessment of students in this discipline is presented on the Educational Portal of the PRMU, specify a link to this electronic resource.*

<https://sdo.pimunn.net/course/view.php?id=3945>

Entry /current control is carried out by the discipline teacher when conducting classes in the form of: tests, situational tasks and projects

4.1. situational Tasks for the assessment of competence: UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)

(A) Download a genotype and phenotype dataset of your choosing. Using PLINK (<http://pngu.mgh.harvard.edu/~purcell/plink/>) or a statistical program such as R (<http://www.r-project.org/>), calculate the association (using a Fisher's exact test) between <Trait> and each SNP. After Bonferroni correction, does any SNP reach genome-wide significance? (B) Does using a different correction method such as Benjamini or False Discovery Rate (FDR) result in any more significant SNPs?

(A) Use a pharmacogenomic database (such as PharmGKB) to find genes that may interact with metformin. (B) Are any of these genes known to interact with other drugs? Which drugs? (C) Bonus question: Are any of these drugs related (by structure or function) to metformin?

(A) Implement a warfarin dosing equation (e.g. the one found in [15]). If you have a personal genotype, input your information and calculate your optimal starting warfarin dose; otherwise, calculate the optimal dose (as predicted by both the clinical and pharmacogenetic algorithms) for a 66-year old Caucasian (175 cm, 75 kg), not taking amiodarone or enzyme inhibitors, who is rs9923231 TT and CYP2C9 \*2/\*2? (B) Would the clinical algorithm have over- or under-estimated his (or your) dose and what are the potential consequences of such an error?

You are a physician and would like to prescribe simvastatin. What parts of the genome would you want interrogated to know about prescribing this drug and why?

Read about the clinical uses of a whole genome or exome in healthy and individuals. How can pharmacogenomics be directly applied in a clinical setting?

4.2. Test tasks Tasks for the assessment of competence: UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1):

Question	Competence code (according to the WPD)
<p>1. Which of the one is referred to as the three-dimensional shape of a protein?  a) secondary structure  <u>b) primary structure</u>  c) tertiary structure  d) quaternary structure</p> <p>2. Which technique prompted the gene therapy?  a) <u>DNA transform</u>  b) germline manipulation  c) retroviral gene therapy  d) electroporation</p> <p>3. Which of the following are examples of genetic polymorphisms?  a) Glutathione S-transferase  b) Dihydropyrimidine dehydrogenase  c) UDP-glucuronosyl transferase  <u>d) all of these</u></p> <p>4. Successful gene therapy face which of the following obstacle?  a) lack of research effort  <u>b) inefficient gene delivery</u>  c) inability to identify genetic defects  d) none of these</p> <p>5. Which of the following is most commonly occurring variant in human genome?  a) defective gene splicing  b) premature stop codon.  c) nucleotide base insertion.  <u>d) single-nucleotide polymorphism</u></p> <p>6. Among all of these which of the following gene increases the risk of thrombosis?  a) tamothrombin  b) mecathrombin  <u>c) prothrombin</u>  d) vorithrombin</p> <p>7. CYP2D6 polymorphism can affect  a) drug delivery  <u>b) toxicity</u>  c) drug interaction potential  d) all of these</p> <p>8. Which gene predict the muscle toxicity?  <u>a) SLCO1B1</u>  b) ABAB2  c) LDLR  d) none of these</p> <p>9. Which of the following are the sites for gene variations?  <u>a) drug target protein</u>  b) drug transport protein  c) drug metabolize enzyme  d) all of these</p> <p>10. In which of the following mutation homologous repeat involve?  <u>a) Large deletions</u></p>	<p>UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)</p>

b) Nonsense mutations c) Splicing mutations d) Missense mutations 11. Which mutation occurs due to uv exposure? a) chromosome breakage b) chromosome inversion <u>c) thymidine dimer</u> d) none of these 12. Which RNA is included in splicosome? a) rRNA b) mRNA c) siRNA <u>d) snRNA</u>	
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4.3. list of topics for individual project: UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)

1. "The history of the formation of pharmacogenetics as a science"
2. "The importance of pharmacogenetic testing for rational dosage of medicines".
3. Genetic polymorphism of target organ cells".
4. Pharmacogenetics in psychopharmacology. Pharmacogenetic bases of differentiated use of psychotropic drugs".
5. "Pharmacogenetic bases of differentiated use of steroid and nonsteroidal anti-inflammatory drugs".
6. Pharmacogenetic bases of differentiated use of antibiotics, antiviral and antifungal drugs".

4.4. Tasks (assessment tools) for the credit

The full package of examination tasks/tasks is given: UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)

### 5. The content of the assessment tools of mid-term assessment

Mid-term assessment is carried out in the form of a credit

*The content of the assessment tool (test questions.)*

5.1 The list of control tasks and other materials necessary for the assessment of knowledge, skills and work experience

Question	Competence code (according to the WPD)
1. Which of the following is not true about pharmacogenetics? a. It is the branch of pharmacology that seeks to understand the genetic basis for differences in drug responsiveness among humans. <u>b. Pharmacogenetics is defined as the investigation of variations in DNA and RNA characteristics as related to drug response.</u> c. Pharmacogenetics is defined by the US Food and Drug Administration (FDA) as the investigation of the role of variations in DNA sequence on drug response. d. Pharmacogenetics and pharmacogenomics are areas of intense interest and development within the biotechnology and pharmaceutical industries.	UC-1 (IUC-1.2, IUC-1.3), PC-7 (IPC-7.1)
2. Which of the following is not true about codeine? a. Codeine, one of the commonly prescribed opioid analgesics for pain in dentistry. b. Codeine is a prodrug and its activation to morphine depends on CYP2D6 enzyme. c. If a patient inherits a deficiency in CYP2D6 or the m-opioid response system, it is unlikely that standard doses of codeine will be of therapeutic benefit.	

<p>d. <u>Codeine is an effective analgesic in all genetic subset of the population.</u></p> <p>3. Which of the following is not true about genotype?</p> <p>a. <u>A biological or measurable expression of the genetic trait.</u></p> <p>b. An individual's genotype is a genetic trait defined by the DNA sequences (i.e., alleles) inherited from the mother and the father.</p> <p>c. An individual can inherit two copies of the same allele (homozygous genotype) or a different allele from each of the parents (heterozygous genotype).</p> <p>d. Many methods to determine the genotype have been developed in the past two decades, including restriction fragment length polymorphism analysis, allele-specific amplification, and DNA sequencing.</p> <p>4. What are monogenic phenotypes?</p> <p>a. Phenotypes that derive from some combination of variations in multiple genes.</p> <p>b. <u>Phenotypes that derive from genetic variations in a single gene.</u></p> <p>c. Phenotypes that derive from genetic variations in all the genes.</p> <p>d. Phenotypes that do not have any variation in gene.</p> <p>5. The frequency of specific alleles, genotypes, and phenotypes for drug-metabolizing enzymes varies widely with ethnic origin.</p> <p>a. <u>True.</u></p> <p>b. False.</p> <p>c. The statement is partially true.</p> <p>d. The statement is true but not for drug-metabolizing enzymes.</p> <p>6. Which of the following is not true about genetic polymorphism?</p> <p>a. It is anticipated that genetic polymorphism is present in all the drug-metabolizing enzymes.</p> <p>b. <u>It has been proved that genetic polymorphism is present in all the drug-metabolizing enzymes.</u></p> <p>c. Many of the genetic polymorphisms are already known to be important in therapeutics.</p> <p>d. CYP2D6 shows genetic polymorphism.</p> <p>7. N-acetylation is an important phase II conjugation reaction for many drugs, EXCEPT</p> <p>a. procainamide.</p> <p>b. dapsone.</p> <p>c. hydralazine.</p> <p>d. <u>metoclopramide.</u></p> <p>8. The acetylation polymorphism was originally discovered by studying the development of peripheral neuropathy in patients administered</p> <p>a. rifampicin.</p> <p>b. <u>isoniazid.</u></p> <p>c. dapsone.</p> <p>d. sulfonamides.</p> <p>9. Which of the following statements is wrong?</p> <p>a. N-acetylation of aromatic amine-containing and hydrazine-containing drugs are catalyzed by N-acetyltransferase isozymes.</p> <p>b. <u>Genetic polymorphisms have been identified only in NAT1.</u></p>	
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- c. Acetylator genotypes derived from more than 25 different NAT2 alleles have been identified in humans.
- d. Eleven identified SNPs in the NAT2 gene affect protein expression or stability or both.

10. What is the cytochrome P450 (CYP) system?

- a. It is a family of microsomal enzymes with nonselective but frequently overlapping substrate specificities.
- b. It is a family of microsomal enzymes with selective but frequently nonoverlapping substrate specificities.
- c. It is a family of microsomal enzymes with selective but frequently overlapping substrate specificities.
- d. It is a family of microsomal enzymes with nonselective but frequently nonoverlapping substrate specificities.

11. Which are the three drug oxidation polymorphisms that have received the most clinical attention?

- a. CYP2D6, CYP2C9, and CYP2C19.
- b. CYP2D6, CYP2C9, and CYP27A1.
- c. CYP2D6, CYP2C9, and CYP4V2.
- d. CYP2D6, CYP2C9, and CYP11B2.

12. Which of the following enzymes is required for tamoxifen to be biotransformed to the potent antiestrogen endoxifen?

- a. CYP2C9.
- b. CYP2D6.
- c. CYP2C19.
- d. CYP1B1.

13. Enzyme CYP2C9 does not catalyze the oxidation of

- a. warfarin.
- b. codeine.
- c. phenytoin.
- d. losartan.

14. Warfarin is a difficult drug to use because of many factors. Which of the following factors does not contribute to warfarin metabolism?

- a. Genetic polymorphisms in CYP2C9.
- b. Genetic polymorphisms in CYP4F2 (which oxidizes vitamin K).
- c. Vitamin K epoxide reductase (VKORC1, the target of warfarin inhibition).
- d. Homocysteine levels.

15. Which of the following is not true about CYP2C19?

- a. CYP2C19 catalyzes the oxidation of mephenytoin.
- b. CYP2C19 catalyzes the oxidation of omeprazole.
- c. Individuals with genetic deficiencies may experience increased sedation and ataxia with the anticonvulsant mephenytoin.
- d. Individuals with genetic deficiencies may experience decreased therapeutic efficacy with omeprazole used for the treatment of peptic ulcer.

16. Which of the following is not true about plasma cholinesterase?

- a. Plasma cholinesterase catalyzes the hydrolysis of choline esters.
- b. Individuals with genetic deficiency in plasma cholinesterase experience prolonged apnea when treated with succinylcholine.

c. The primary atypical form of plasma cholinesterase possesses an SNP that changes an amino acid (aspartic acid to glycine) in the anionic site of the esterase, reducing its affinity for succinylcholine.

d. Succinylcholine is frequently used to produce muscular relaxation for endotracheal intubation.

17. Thiopurine S-methyltransferase (TPMT) catalyzes the deactivating S-methylation of the following drugs, EXCEPT

a. 6-mercaptopurine.

b. 6-thioguanine.

c. omeprazole.

d. azathioprine.

18. Genetic variants of the multidrug resistance transporter P-glycoprotein, the product of the MDR1 gene, have been associated with altered transport, efficacy, and toxicity of all the following, EXCEPT

a. digoxin.

b. tacrolimus.

c. irinotecan.

d. azathioprine.

19. Malignant hyperthermia (MH) can present with all of the following manifestations, EXCEPT

a. bradycardia.

b. hypercarbia.

c. hypoxia.

d. tachycardia.

20. Which of the following drugs is given in acute attack of malignant hyperthermia?

a. Atropine.

b. Adrenaline.

c. Diazepam.

d. Dantrolene.

21. Which of the following is not true about uridine diphosphate glucuronosyltransferase (UGT)?

a. UGT catalyzes the glucuronidation of bilirubin and various drugs and xenobiotics.

b. The UGT1A family of enzymes is represented in the genome by a series of six invariant exons.

c. UGT enzyme levels are regulated primarily through transcriptional control and genetic variation in promoter structure influences transcription rate.

d. Individuals with genetic polymorphism in UGT1A1 have been shown to experience increased toxicity (myelosuppression and diarrhea) with the use of irinotecan.

22. Which of the following is used extensively during chemotherapy of solid tumors?

a. 5-Fluorouracil.

b. Azathioprine.

c. Dantrolene.

d. Efavirenz.

<p>23. Patients with genetic deficiency of dihydropyrimidine dehydrogenase have</p> <p>a. a 70% lower clearance of 5-fluorouracil and may experience severe toxicity from modest doses.</p> <p>b. an 80% lower clearance of 5-fluorouracil and may experience severe toxicity from modest doses.</p> <p><u>c. a 90% lower clearance of 5-fluorouracil and may experience severe toxicity from modest doses.</u></p> <p>d. a 60% lower clearance of 5-fluorouracil and may experience severe toxicity from modest doses.</p> <p>24. The individuals who are homozygous for the UGT1A1*28 allele are at increased risk for which of the following conditions after initiation of irinotecan treatment?</p> <p>a. Lymphocytopenia.</p> <p>b. Anemia.</p> <p><u>c. Neutropenia.</u></p> <p>d. Thrombocytopenia.</p> <p>25. Which of the following is not true about b2-adrenergic receptor?</p> <p>a. b2-Adrenergic receptor genotype variation has been shown to affect therapeutic response to b2-selective agonists such as albuterol.</p> <p>b. Polymorphisms in b receptors potentially influence drug treatment of cardiovascular diseases.</p> <p>c. b2 receptor variant is associated with lower systemic vascular resistance and a greater vasodilatory response.</p> <p><u>d. Individuals with this b2 receptor variant might not be sensitive to a vasodilator (e.g., captopril) acting via another mechanism, secondary to the altered systemic vascular tone.</u></p>	
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## 6. Criteria for evaluating learning outcomes

*For the credit*

Learning outcomes	Evaluation criteria	
	Not passed	Passed
<b>Completeness of knowledge</b>	The level of knowledge is below the minimum requirements. There were bad mistakes.	The level of knowledge in the volume corresponding to the training program. Minor mistakes may be made
<b>Availability of skills</b>	Basic skills are not demonstrated when solving standard tasks. There were bad mistakes.	Basic skills are demonstrated. Typical tasks have been solved, all tasks have been completed. Minor mistakes may be made.
<b>Availability of skills (possession of experience)</b>	Basic skills are not demonstrated when solving standard tasks. There were bad mistakes.	Basic skills in solving standard tasks are demonstrated. Minor mistakes may be made.
<b>Motivation (personal attitude)</b>	Educational activity and motivation are poorly expressed, there is no willingness to solve the tasks qualitatively	Educational activity and motivation are manifested, readiness to perform assigned tasks is demonstrated.

<b>Characteristics of competence formation*</b>	The competence is not fully formed. The available knowledge and skills are not enough to solve practical (professional) tasks. Repeated training is required	The competence developed meets the requirements. The available knowledge, skills and motivation are generally sufficient to solve practical (professional) tasks.
<b>The level of competence formation</b>	Low	Medium/High

*For testing:*

Mark "5" (Excellent) - points (100-90%)

Mark "4" (Good) - points (89-80%)

Mark "3" (Satisfactory) - points (79-70%)

*Less than 70% – Unsatisfactory – Mark "2"*

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